NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES (NIAID)
Division of Acquired Immunodefiency Syndrome (DAIDS)
Network Leadership Meeting
September 17, 2003
Hilton Hotel, New York, New York
Concourse A

Meeting Summary

Welcome **E. Tramont**

Dr. Tramont welcomed the group and thanked everyone for attending.
He noted that in the face of a level budget, DAIDS has to be more efficient with research dollars, particularly as the epidemic continues to expand especially in resource poor developing countries. This is important as DAIDS re-competes its major clinical networks but also because of collaborations and research activities, such as DOD, CDC, ESPRIT, ADRIP, PHIDISA. The first meeting in June was a discussion on operations. This meeting will focus on the science. DAIDS will convene another meeting to discuss recompetition. Jonathan Kagan will chair this meeting.

Update and Review **J. Kagan**
Dr. Kagan briefly gave a timeline of the past meetings (Oct 2001 and November 2002).
The most recent Network Leadership meeting in June 2003 focused on the structuring of clinical trial, networks placing form before function. At that meeting, the leadership group discussed candidate models for integration at the operational level. The discussion today will focus on integration at the scientific level

Developing Scientific Agenda **P. Johnston and S. Lehrman**

- *Stop New Infections*
- *Protecting the uninfected*
- *Continue to pursue innovative translational research*
- *Reducing the infectiousness of infected*

Discussion focused on the following issues:

- *There should not be a separate pediatric and adult treatment research agenda. All adult sites should have a peds site and vice versa. MTCT trials should be conducted along with treatment of the adult (family) population.*

- *How can the therapeutic and preventive vaccine agendas be integrated? One area of intersection might be the selection of new vaccines for both therapeutic and preventive studies. Both domestically and internationally, this will be an important aspect of the research agenda in the next five years.*

- *The broad scientific questions have not changed in the last five years. There have been incremental advances in the therapies available to address the questions. Second and third generation ARTs have improved pharmacology and toxicology and enhanced the resistance*

profile. Overall the domestic research agenda is focused on how to better use the "improved" drugs in three areas:

- *When to start and what to start with?*
- *When to switch and how to monitor and combat resistance and complications of ART*
- *How to salvage multiple resistant patients*

- *Operational (optimal vs. deliverable) research. The design of the study should be incremental and be able to answer several different questions*

- *Discussion on developing countries. The stakes are higher in resource poor countries. If the group's work is to be relevant, local leadership involvement is needed. Furthermore, there must be a way to link up with national policy people in the region. (This can only be an indirect link since public health policy is not the purview of the NIH)*

    - *Emphasize (but not exclusively) alliances with the countries in the President's initiative. Get a list of collaborations within the Networks in the 14 countries and build pressure from within each country for a research agenda. Ask the local people to help define a research agenda.*
    - *Use the collaborators in the 14 countries as a pilot project to begin Network integration at specific sites with the goal of empowering/expanding activities at their sites. This will help establish a research base so that these international investigators have a voice within their countries to advocate for research as part of their countries' plan*

- *Attention needs to be given to the treatment component of vaccine prevention studies. The operational requirements for all clinical trials are the same; therefore, integrated clinical trial sites should be fostered rather than specific prevention or treatment trial sites.*

- *Is there a need for large multi-center trials? These trials take a long time to complete and follow a regulatory pre-licensure paradigm, with many checks and balances that delay implementation.*

- *How does one begin to look at Opportunistic Infections in Resource poor developing countries (RPDC's)? Do we expect the CDC to do this? Or the Networks? How would NIAID look at it? The international research agenda clearly needs to link systems that can provide treatment for OIs, TB and malaria.*

- *Another area of collaboration discussed was the impact of prevention and ART on transmission.*

    - *Perhaps a 052 type of study (a collaboration of HPTN & AACTG)?*
    - *At the individual level, what would be the impact of treatment?*
    - *How do you introduce preventive, behavioral interventions in ART clinical trials?*
    - *Can we take a cohort of individuals to whom ART may be provided and look at the impact of behavioral intervention?*
    - *Are women receiving ART likely to use birth control or not and what is the perinatal transmission?*
    - *People who are not taking ART are primary sources of new infection. Can look at other STDs as end point.*

- *Domestically, collaboration between the CDC and ART clinics?*
- *SMART study, which needs to enroll, will determine impact of therapy on prevention with a transmission infection endpoint*
- *ESPRIT – IL2 w/o ART opportunity to pilot prevention/behavioral*
- *PACTG, HPTN, HVTN – The question of how to use ART therapy to evaluate the impact on transmission is part of the prevention/treatment agenda. Three networks are conducting trials addressing this question*

- *Domestically all networks are facing enrollment issues so there is a need to increase capacity by expanding into the international arena. (Some prevention trials will require an enrollment of 50,000 volunteers)*

- *What is the best way to come up with these scientific priorities? Is it better to start from bottom up? Should we have coordination from an operational standpoint? Is it better to discuss these issues in smaller groups?*

DAIDS staff challenged the therapeutics and prevention networks to putting additional effort into creating an integrated portfolio of studies to address this question and to determine whether the role of ART in the prevention of HIV transmission was being sufficiently addressed.

Participants agreed with the outline of scientific priorities presented; however there was concern that the list was very general. The Network leadership felt that specific priorities needed to be defined to allow for greater debate.

DAIDS staff summarized the group's consensus about developing specific scientific priorities and the leadership's greater concern with *operational challenges* facing integration.

Below is a list of the areas of operational integration identified at this and past network leadership meetings. These are perhaps areas around which DAIDS might convene consultations/working groups as a way to solicit input not only from the network leadership but also from the community and other investigators.

- Laboratories (safety, virology, immunology, diagnostic, QC)
- Specimen management (storage, shipping)
- Support training: GCP, OHRP, QA/QC, regulatory, project management, AE reporting
- Meetings – across networks

Future Discussion Topics
- Clinical Site Selection
- International Site Funding
- Community Resources and outreach

Other activities that would allow for such working groups include:

- Voluntary Counseling & Testing (VCT), care, treatment and prevention programs

- NIAID (CIPRA, non-network studies)
- Non –NIAID (NIH IC's, other organizations)
- Scientific Integration

Responses to DAIDS summary:

- The danger in setting priorities is that each network will have a bias because it needs to answer to different constituencies. We need to come up with efficiencies based out of operational issues.

- The amount of money that is allocated to international activities was raised?

- Specific ideas should be developed in areas of overlap. For instance, shared laboratories for prevention and treatment research.

- Establish centers of excellence internationally.

- Utilize a family centered approach to intervention.

- Broad national issues need to be taken into consideration.

- Start with a couple of pilot programs that seek to integrate selected operational activities. How these pilot projects will be selected needs to be defined.

- Ask regional questions. There is no need to set up international studies, multi center, multi country studies would work well.

- Create infrastructure, i.e. one specialist from each network who will oversee management of network.

ACTION ITEMS:

- DAIDS needs to put together an RFA
  Suggestions:
  - DAIDS could form teams of staff and investigators to formulate models for key operational processes.
  - Possible areas of scientific collaboration:
    - Impact of ART on prevention;
    - MTCT issue
  - Could non-conflicted people be chosen to serve on review to select CRO

- DAIDS to send minutes to Network leadership *ASAP*